General

Guideline Title

Paraproteinaemic demyelinating neuropathies.

Bibliographic Source(s)

Hadden RD, Nobile-Orazio E, Sommer C, Hahn AF, Illa I, Morra E, Pollard J, Lunn MP, Bouche P, Cornblath DR, Evers E, Koski CL, Leger JM, Van den Bergh P, van Doorn P, van Schaik IN. Paraproteinaemic demyelinating neuropathies. In: Gilhus NE, Barnes MP, Brainin M, editor(s). European handbook of neurological management. 2nd ed. Vol. 1. Oxford (UK): Wiley-Blackwell; 2011. p. 351-61. [65 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of paraproteinemic demyelinating neuropathies. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Soc. J Peripher Nerv Syst 2006 Mar;11(1):9-19.

Recommendations

Major Recommendations

The levels of evidence (Class I-IV) supporting the recommendations and ratings of recommendations (A-C, Good Practice Point [GPP]) are defined at the end of the "Major Recommendations" field.

Investigation and Classification of the Paraproteins

The table below suggests investigations to be considered in all patients with a paraprotein. Serum immunofixation electrophoresis (SIFE) should be performed in patients with a known paraprotein to define the heavy- and light-chain types, in patients with acquired demyelinating neuropathies, and in patients in whom a paraprotein is suspected but not detected by standard serum protein electrophoresis (SPEP).

Table. Investigation of a Paraprotein
The following should be considered in all patients with a paraprotein: a. Serum immunofixation electrophoresis b. Physical examination for peripheral lymphadenopathy, hepatosplenomegaly, macroglossia, and signs of polyneuropathy, organomegaly, endocrinopathy, M band, and skin changes (POEMS syndrome) (see section "Other neuropathy syndromes associated with

Table. Investigation of a Paraprotein (paraproteinaemia" in the original guideline document)

c. Full blood count, renal and liver function, calcium, phosphate, erythrocyte sedimentation rate, C-reactive protein, uric acid, beta 2-microglobulin, lactate dehydrogenase, rheumatoid factor, serum cryoglobulins
d. Total immunoglobulin G (IgG), IgA, IgM concentrations
e. Serum free light chains
f. Random urine collection for the detection of Bence-Jones protein (free light chains), and, if positive, 24 h urine collection for protein quantification
g. Radiographic x-ray skeletal survey (including skull, pelvis, spine, ribs, long bones) to look for lytic or sclerotic lesions. Part or all of this may be replaced by computed tomography (CT), which is more sensitive but involves greater radiation exposure except where low-dose whole body CT is available. If the index of suspicion is high, CT and/or magnetic resonance imaging (MRI) of the spine, pelvis or whole body, and perhaps whole body fluorine-18-labeled deoxyglucose positron emission tomography (FDG-PET)/CT, may be considered.
h. Ultrasound or CT of chest, abdomen, and pelvis (to detect lymphadenopathy, hepatosplenomegaly, or malignancy)
i. Serum vascular endothelial growth factor (VEGF) levels if POEMS syndrome suspected
j. Consultation with a haematologist and consideration of bone marrow examination

Is the Paraprotein Causing the Neuropathy?

Table. Causal Relationship between Paraprotein and Demyelinating Neuropathy

1. *Highly probable* if immunoglobulin M (IgM) paraprotein (monoclonal gammopathy of uncertain significance [MGUS] or Waldenström's) and:
    a. High titers of IgM anti-myelin-associated glycoprotein (anti-MAG) or anti-GQ1b antibodies, or
    b. Nerve biopsy shows IgM or complement deposits on myelin, or widely spaced myelin on electron microscopy

2. *Probable* if either:
    a. IgM paraprotein (MGUS or Waldenström's) with high titers of IgM antibodies to other neural antigens (GM1, GD1a, GD1b, GM2, sulphatide, etc.), and slowly progressive predominantly distal symmetrical sensory neuropathy, or
    b. IgG or IgA paraprotein and nerve biopsy evidence (as in1b but with IgG or IgA deposits)

3. *Less likely* when any of the following are present in a patient with MGUS and without anti-MAG antibodies (diagnosis may be described as 'chronic inflammatory demyelinating polyradiculoneuropathy [CIDP] with coincidental paraprotein'):
    a. Time to peak of neuropathy <6 months
    b. Relapsing/remitting or monophasic course
    c. Cranial nerves involved (except chronic ataxic neuropathy with ophthalmoplegia, IgM monoclonal gammopathy, cold agglutinins, and disialoganglioside [CANOMAD])
    d. Asymmetry
    e. History of preceding infection
    f. Abnormal median with normal sural sensory action potential
    g. IgG or IgA paraprotein without biopsy features in 2b

Cerebrospinal Fluid and Nerve Biopsy

Cerebrospinal fluid (CSF) examination and nerve biopsy may be helpful in selected circumstances (see table, below, [GPP]) but are usually not necessary if there is clearly demyelinating physiology with monoclonal gammopathy of uncertain significance (MGUS).

Table. Cerebrospinal Fluid (CSF) Examination and Nerve Biopsy

1. CSF examination is most likely to be helpful in the following situations:

Table. Cerebrospinal Fluid (CSF) Examination and Nerve Biopsy

a. In patients with borderline demyelinating or axonal electrophysiology or atypical phenotype, where the presence of raised CSF protein would help suggest that the neuropathy is immune-mediated
b. The presence of malignant cells would confirm lymphoproliferative infiltration

2. Nerve biopsy (usually sural nerve) is most likely to be helpful when the following conditions are being considered:
    a. Amyloidosis
    b. Vasculitis (e.g., due to cryoglobulinaemia)
    c. Malignant lymphoproliferative infiltration of nerves, or
    d. Immunoglobulin M paraproteinaemic demyelinating neuropathy (IgM PDN) with negative anti-myelin-associated glycoprotein (anti-MAG) antibodies, or IgG or IgA PDN with a chronic progressive course, where the discovery of widely-spaced myelin on electron microscopy or deposits of immunoglobulin and/or complement bound to myelin would support a causal relationship between paraprotein and neuropathy.

However, clinical decisions on treatment are often made without a biopsy.

Treatment of Paraproteinaemic Demyelinating Neuropathy (PDN)

Treatment of IgM PDN

1. In patients without significant disability or haematological reason for treatment, there is no evidence that immunosuppressive or immunomodulatory treatment is beneficial. Patients may be offered symptomatic treatment for tremor and paraesthesiae, and reassurance that symptoms are unlikely to worsen significantly for years.
2. In patients with significant chronic or progressive disability, immunosuppressive or immunomodulatory treatment may be considered, although none is of proven efficacy, and there is no consensus on which treatment to use first. Intravenous immunoglobulin (IVIg) or plasma exchange (PE) should be considered, especially in patients with rapid worsening or clinically similar to typical CIDP, although any benefit may be only short term and repeated treatments may be required. In attempts to achieve longer-term benefit (or in patients unresponsive to IVIg or plasma exchange), clinicians have used rituximab, cyclophosphamide with prednisolone, fludarabine, and chlorambucil. All remain unproven and all have risks which must be balanced against any possible benefits.
3. More research on pathogenesis and treatment is needed.

Treatment of IgG and IgA PDN

In patients with a CIDP-like neuropathy, the detection of IgG or IgA MGUS does not justify a different therapeutic approach from CIDP without a paraprotein.

Treatment of Signs of Polyneuropathy, Organomegaly, Endocrinopathy, M and, Band Skin Changes (POEMS)

This is a malignant condition which should be managed in consultation with a haemato-oncologist. The 2008 Cochrane Review concluded: 'Despite the absence of evidence from randomized trials, the review authors consider it clinically logical that the foundation of treatment is radiation for patients with a solitary osteosclerotic lesion …, and high-dose melphalan with autologous peripheral blood stem cell transplantation for patients under 65 years with diffuse disease as demonstrated by multiple bone lesions or documented clonal plasma cells in iliac crest biopsy. Lenalidomide/thalidomide, anti-vascular endothelial growth factor (VEGF) monoclonal antibody (bevacizumab), and conventional chemotherapy with melphalan or cyclophosphamide may also be treatment options'.

Definitions:

Evidence Classification Scheme for a Diagnostic Measure

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a 'gold standard' for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by 'gold standard') compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum,

and where test is applied in a blinded evaluation

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls)

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
c. Exclusion/inclusion criteria are clearly defined
d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

Rating of Recommendations for a Diagnostic Measure

Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (established as possibly useful/predictive or not useful/predictive) requires at least two convincing class III studies.

Rating of Recommendations for a Therapeutic Intervention

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Good Practice Point When only class IV evidence was available but consensus could be reached, the task force offered advice as Good Practice Points.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Paraproteinaemic demyelinating neuropathy (PDN)

Note: This guideline concentrates on the demyelinating neuropathies. Paraproteinaemic axonal neuropathies are mentioned briefly.

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Neurology

Oncology

Intended Users

Physicians

Guideline Objective(s)

- To construct clinically useful guidelines for the diagnosis, investigation, and treatment of patients with both a demyelinating neuropathy and a paraprotein (paraproteinaemic demyelinating neuropathy [PDN]), based on the available evidence and, where evidence was not available, consensus
- To revise the original 2006 guideline on PDN

Target Population

Patients presenting with paraproteinaemic demyelinating neuropathy (PDN)

Interventions and Practices Considered

Diagnosis/Evaluation

1. Investigation of a paraprotein including:
    - Serum immunofixation electrophoresis (SIFE)
    - Physical examination and assessment of signs and symptoms
    - Full blood count, renal and liver function, calcium, phosphate, erythrocyte sedimentation rate, C-reactive protein, uric acid, beta 2-microglobulin, lactate dehydrogenase, rheumatoid factor, serum cryoglobulins
    - Total immunoglobulin G (IgG), IgA, IgM concentrations
    - Serum free light chains
    - Random urine collection for the detection of Bence Jones protein (free light chains) and 24-h urine collection for protein quantification
    - Radiologic x-ray skeletal survey (skull, pelvis, spine, ribs, long bones)
    - Serum vascular endothelial growth factor (VEGF) levels
    - Ultrasound or computed tomography (CT) of abdomen and chest and other imaging studies
    - Consultation with a haematologist

2. Cerebrospinal fluid examination
3. Nerve biopsy

Management/Treatment

1. IgM paraproteinaemic demyelinating neuropathy (PDN)
    - Withholding immunosuppressive or immunomodulatory treatment and providing symptomatic treatment for tremor and paraesthesiae in patients without significant disability
    - Intravenous immunoglobulin (IVIg)
    - Plasma exchange (PE)
    - Immunosuppressive or immunomodulatory treatment in patients with significant disability
2. IgG and IgA PDN
    - Therapeutic approach similar to the approach in chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
3. Signs of polyneuropathy, organomegaly, endocrinopathy, M band, and skin changes (POEMS)
    - Consultation with haemato-oncologist
    - Local radiation
    - Melphalan with autologous peripheral blood stem cell transplantation
    - Lenalidomide/thalidomide, anti-VEGF monoclonal antibody (bevacizumab), and conventional chemotherapy with melphalan or cyclophosphamide

Major Outcomes Considered

Sensitivity of diagnostic tests
Effectiveness of treatment

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The task force members searched MEDLINE and the Cochrane Library on 1 May 2009 for articles on 'paraprotein(a)emic demyelinating neuropathy' and 'diagnosis' or 'treatment' or 'guideline' and used the personal databases of task force members.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Evidence Classification Scheme for a Diagnostic Measure

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a 'gold standard' for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by 'gold standard') compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls)

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
c. Exclusion/inclusion criteria are clearly defined
d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Recommendations were classified as levels A to C (see the "Rating Scheme for the Strength of the Recommendations" field). When only Class IV evidence was available but consensus could be reached, the task force has offered advice as Good Practice Points (GPP). The original 2006 guideline was revised iteratively until unanimous consensus was reached.

Rating Scheme for the Strength of the Recommendations

Rating of Recommendations for a Diagnostic Measure

Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (established as possibly useful/predictive or not useful/predictive) requires at least two convincing class III studies.

Rating of Recommendations for a Therapeutic Intervention

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Good Practice Point When only class IV evidence was available but consensus could be reached, the task force offered advice as Good Practice Points.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Peer Review

Description of Method of Guideline Validation

The guidelines were validated according to the European Federation of Neurological Societies (EFNS) criteria (see the "Availability of Companion Documents" field).

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for selected recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis, investigation, and treatment of paraproteinaemic demyelinating neuropathy (PDN)

Potential Harms

- Computed tomography (CT) is more sensitive than x-ray but involves greater radiation exposure
- Adverse effects of medications

Qualifying Statements

Qualifying Statements

This guideline provides the view of an expert task force appointed by the Scientific Committee of the European Federation of Neurological Societies (EFNS). It represents a peer-reviewed statement of minimum desirable standards for the guidance of practice based on the best available evidence. It is not intended to have legally binding implications in individual cases. This guideline is not intended to have implications regarding reimbursement.

Implementation of the Guideline

Description of Implementation Strategy

The European Federation of Neurological Societies has a mailing list and all guideline papers go to national societies, national ministries of health, World Health Organisation, European Union, and a number of other destinations. Corporate support is recruited to buy large numbers of reprints of the guideline papers and permission is given to sponsoring companies to distribute the guideline papers from their commercial channels, provided there is no advertising attached.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Hadden RD, Nobile-Orazio E, Sommer C, Hahn AF, Illa I, Morra E, Pollard J, Lunn MP, Bouche P, Cornblath DR, Evers E, Koski CL, Leger JM, Van den Bergh P, van Doorn P, van Schaik IN. Paraproteinaemic demyelinating neuropathies. In: Gilhus NE, Barnes MP, Brainin M, editor(s). European handbook of neurological management. 2nd ed. Vol. 1. Oxford (UK): Wiley-Blackwell; 2011. p. 351-61. [65 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2006 Mar (revised 2011)

Guideline Developer(s)

European Academy of Neurology - Medical Specialty Society

Source(s) of Funding

European Federation of Neurological Societies

Guideline Committee

European Federation of Neurological Societies Task Force on Paraproteinaemic Demyelinating Neuropathies

Composition of Group That Authored the Guideline

Task Force Members: R. D. M. Hadden, King's College Hospital, London, UK; E. Nobile-Orazio, IRCCS Humanitas Clinical Institute, University of Milan, Italy; C. Sommer, University of Würzburg, Germany; A. F. Hahn, University of Western Ontario, London, Canada; I. Illa, Hospital Sta. Creu i Sant Pau, Barcelona, Spain; E. Morra, Niguarda Hospital, Milan, Italy; J. Pollard, University of Sydney, Australia; M. P. T. Lunn, National Hospital for Neurology and Neurosurgery, Queen Square, London, UK; P. Bouche, CHU Pitié-Salpêtrière, Paris, France; D. R. Cornblath, Johns Hopkins University, Baltimore, MD, USA; E. Evers, Guillain-Barré Syndrome Support Group of the UK; C. L. Koski, University of Maryland, Baltimore, USA; J.-M. Léger, Faculté de Médecine Pitié-Salpêtrière, Paris, France; P. Van den Bergh, Cliniques St.-Luc, Université Catholique de Louvain, Brussels, Belgium; P. van Doorn, Erasmus Medical Centre, Rotterdam, The Netherlands; I. N. van Schaik, Academic Medical Centre, Amsterdam, The Netherlands

Financial Disclosures/Conflicts of Interest

The following authors have reported conflicts of interest as follows:

D. Cornblath: personal honoraria from Merck, Pfizer, Mitsubishi Pharma, Sangamo, Sanofi-Aventis, Bristol-Myers Squibb, Eisai, Octapharma, Sun Pharma, Acorda, DP Clinical, Exelixis, Geron, Johnson & Johnson, Genyzme, Cebix, Abbott, CSL Behring, Bionevia, Schwarz Biosciences, Avigen, FoldRx, GlaxoSmithKline.

R. D. M. Hadden: personal honoraria from Janssen-Cilag and Baxter Healthcare.

A. F. Hahn: departmental research grants and personal honoraria from Bayer, Baxter, Biogen-Idec, Talecris.

I. Illa: personal none, departmental research grant from Grifols.

C. Koski: personal honoraria from American Red Cross, Baxter, Bayer, and ZLB-Behring.

J. M. Léger: personal none, departmental research grants or honoraria from Biogen-Idec, Baxter, Laboratoire Français du Biofractionnement (LFB), and Octapharma.

M. Lunn: commissioned to give opinions on IVIg and PE usage by UK Department of Health and received honoraria from Baxter Pharmaceuticals and LFB.

E. Nobile-Orazio, personal honoraria from Kedrion, Grifols, Baxter, and LFB (and he has been commissioned by Kedrion and Baxter to give expert opinions to the Italian Ministry of Health on the use of IVIg in dysimmune neuropathies).

J. Pollard: departmental research grants from Biogen-Idec and Schering.

C. Sommer: personal honoraria from Biogen-Idec and Baxter International Inc.

P. van Doorn: personal none, departmental research grants or honoraria from Baxter and Bayer.

I. N. van Schaik: personal none, unrestricted departmental research grant from Sanquin blood supply foundation.

The other authors have nothing to declare.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of paraproteinemic demyelinating neuropathies. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Soc. J Peripher Nerv Syst 2006 Mar;11(1):9-19.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the European Federation of Neurological Societies (EFNS) Web site .

Availability of Companion Documents

The following is available:

- Brainin M, Barnes M, Baron JC, Gilhus NE, Hughes R, Selmaj K, Waldemar G; Guideline Standards Subcommittee of the EFNS Scientific Committee. Guidance for the preparation of neurological management guidelines by EFNS scientific task forces – revised recommendations 2004. Eur J Neurol. 2004 Sep;11(9):577-81. Electronic copies: Available in Portable Document Format (PDF) from the European Federation of Neurological Societies Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on December 8, 2006. The information was verified by the guideline developer on January 2, 2007. This summary was updated by ECRI Institute on October 8, 2008 following the U.S. Food and Drug Administration advisory on Rituxan (rituximab). This NGC summary was updated by ECRI Institute on February 20, 2012. This summary was updated by ECRI Institute on November 21, 2013 following the U.S. Food and Drug Administration advisory on Arzerra (ofatumumab) and Rituxan (rituximab).

Copyright Statement

This NGC summary is based on the original guideline, which is subject to the Blackwell-Synergy copyright restrictions.

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouseâ„¢ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines

represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.